REMARKS

Claims 1-42, 59-66, and 70-76 are under consideration in the above-referenced patent application and have been rejected under 35 U.S.C. § 103. Applicants respectfully request reconsideration and withdrawal of these rejections in view of the following discussion, and the Declaration of Carl Anthony Blau under 37 C.F.R. § 1.132.

Rejections under 35 U.S.C. § 103

Rejections over Capon et al. in view of Blau et al.

Claims 1-42, 59-66 and 70-76 stand rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,741,899 (Capon et al.) in view of Blau et al. (1997). As explained below, Blau et al. is not valid prior art against the present claims because it represents the inventors' own work and was published less than one year before the priority date to which the present claims are entitled.

Summary of the ground for rejection:

Capon et al. teaches chimeric proteins that comprise a signaling domain and a drug-responsive domain, and describes an experiment to test cell proliferation *in vitro* using an assay in which cells expressing such a chimeric protein are contacted with plates coated with a saturating concentration of an inducer drug (see, for example, Capon et al. at column 42, line 48 to column 43, line 12). In the Office Action of October 6, 2005, the Examiner acknowledged that, in view of the third Blau declaration (filed July 7, 2005), Capon did not teach a concentration of the drug effective in inducing the proliferation of a primary cell type. The Examiner relies on Blau et al. for teaching that varying the concentration of the inducer molecule

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

could identify a concentration capable of inducing dimerization and signaling through the chimeric receptor. In their last amendment, applicants argued that one following the teachings of Capon would not think to combine its teachings with Blau et al. because one would not know why the Capon assay failed to work. However, the Examiner has rejected this argument.

Where the applicant is one of the co-authors of a publication cited against his or her application, he or she may overcome the rejection by filing an affidavit or declaration under 37 C.F.R. § 1.132 establishing that the article is describing applicant's own work. An affidavit or declaration by applicant alone indicating that applicant is the sole inventor and that the others were merely working under his or her direction is sufficient to remove the publication as a reference under 35 U.S.C. 102(a). *In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA 1982). Such a declaration also can remove a publication as a reference under 35 U.S.C. 103(a).

The rejected claims are entitled to a priority date of at least January 9, 1998:

Blau et al. was published in April, 1997, while the present application claims priority from three provisional applications filed January 8, 1998 (USSN 60/070,754), January 9, 1998 (USSN 60/070,893) and October 2, 1998 (USSN 60/102,888). Support for the current claims is found throughout the specifications of USSN 60/070,754 and USSN 60/070,893, both of which were filed less than one year from the publication date of Blau et al. The following discussion establishes that the claims under consideration herein are fully supported at least by the disclosure of USSN 60/070,893, a copy of which is enclosed for the Examiner's convenience.

Specific support for the current claims is found, for example, in the claims of USSN 60/070,893. The claims of USSN 60/070,893, of course, constitute part of the disclosure

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

of that application. Additional support for the current claims is found throughout the specification of USSN 60/070,893.

Claims 2-3, 5-10 and 12-13 of the present application are virtually identical to Claims 2-3, 5-10 and 12-13 of USSN 60/070,893. Furthermore, Claims 15-20, 25-30, 32-42, 47-52, 55, 58-61, 64, 66 and 70-75 of the current application are virtually identical, respectively, to Claims 14-19, 24-29, 31-41, 46-51, 54, 57-60, 61A, 63 and 67-72 of USSN 60/070,893.

Several more of the claims pending herein, namely Claims 1, 4, 11, 21-24, 31, 44-46, 53, 56 and 63 differ only slightly from their corresponding claims in USSN 60/070,893, which are, respectively, Claims 1, 4, 11, 20-23, 30, 43-45, 52, 55, 61 and 62 of USSN 60/070,893. These differences and supplementary support in USSN 60/070,893 are as follows.

Claims 1 and 21 of this application differ from corresponding Claims 1 and 20 of USSN 60/070,893 in that the former include the phrase "wherein the transduction is carried out in vivo or after the cells have been removed from the mammal from which the cells originated." This language is supported in USSN 60/070,893, for example, at page 2, lines 19-20; page 3, lines 6-22; page 3, line 31 to page 4, line 5; page 7, lines 14-15; page 18, line 21 to page 22, line 11; and page 23, lines 27-31;

Present Claims 4, 24, 46 and 56 differ from their corresponding claims in USSN 60/070,893 (Claims 4, 23, 45 and 55) only in that the present claims adds "cord blood cells" to the types of cells recited. USSN 60/070,893 discloses "cord blood cells," for example, at page 3, lines 2-5 and page 22, lines 19-25. Present Claims 63 and 65 also add "cord blood cells" but differs further from their corresponding claims in USSN 60/070,893 (Claims 61 and 62) by adding at the end of the claim the phrase "concentration effective to induce association of

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

two or more fusion proteins." This added language is supported in USSN 60/070,893, for example, at page 2, lines 23-26; page 6, lines 24-26; and page 25, lines 2-3..

Present Claims 11, 31, 53 differ from their corresponding claims in USSN 60/070,893 (Claims 11, 30 and 52) only in that the present claims includes "FGF" in the recited receptors. Use of "FGF" is disclosed in USSN 60/070,893, for example, at page 4, lines 21-26; page 13, lines 19-24; and page 14, lines 4-7 and 28-33.

Claim 14 of the present application has no counterpart in USSN 60/070,893, but support for this claim is found in USSN 60/070,893, for example, at page 3, lines 23-25; page 23, line 30 to page 24, line 1; and page 25, lines 8-9.

Current Claim 22 differs from its counterpart in USSN 60/070,893 (Claim 21) by substituting "exposing the transduced cells to the drug" with "exposing the transduced cells to a concentration of the drug effective to induce association of two or more fusion proteins." Support for current Claim 22 is found in USSN 60/070,893, for example, at page 2, lines 23-26; page 6, lines 24-26; and page 25, lines 2-3.

Current Claims 23 and 45 differ from their counterparts in USSN 60/070,893 (i.e., claims 22 and 44) only in that the current claims recite "embryonic stem cells." Embryonic stem cells are disclosed in USSN 60/070,893, for example, at page 2, line 30 to page 3, line 2 and at page 22, lines 19-24.

Claim 44 of the current application differs from its counterpart in USSN 60/070,893 (Claim 43) in that the current claim includes the phrase "wherein the drug-binding domain comprises at least one amino acid change compared to the most prevalent naturally-occurring amino acid sequence." Support for this added phrase is found in USSN 60/070,893, for example,

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

at page 14, lines 16-19; page 15, line 24 to page 16, line 2; page 16, lines 27-31; and page 17, lines 1-23.

Claim 57 of the present application has no counterpart in the claims of USSN 60/070,893, but support for this claim is found in USSN 60/070,893, for example, at page 3, line 31 to page 4, line 5, and at page 18, line 21 to page 22, line 11.

Claim 62 of the present application, which has no counterpart in the claims of USSN 60/070,893, is supported in USSN 60/070,893, for example, at page 26, lines 16-17.

The foregoing demonstrates the claims under consideration herein are supported under 35 U.S.C. § 112 by the disclosure of USSN 60/070,893, and thus that these claims are entitled to the priority date of at least January 9, 1998, the filing date of USSN 60/070,893.

Some of the authors of Blau et al. made no inventive contribution:

Blau et al. is authored by the inventors C.A. Blau and D.M. Spencer, as well as K.R. Peterson and J.G. Drachman, who are not named as inventors on this application. The attached declaration signed by Dr. Blau (Exhibit A), states that authors K.R. Peterson and J.G. Drachman made no inventive contributions to the disclosure of Blau et al..

As explained in the Declaration of Carl Anthony Blau, submitted herewith, Peterson and Drachman were friends and colleagues of Dr. Blau at the University of Washington at the time the work leading to this invention was underway. As a matter of convenience, Dr. Blau asked Dr. Peterson to perform RNAse protection assays to detect various types of globin transcripts for the project. Peterson was included as an author on the above-mentioned paper to acknowledge these contributions. Dr. Drachman was included as an author on Blau et al. to acknowledge his

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

having run some Western blots at Blau's request using samples that Blau had provided. In view of Exhibit A, Blau et al. should not be considered prior art with respect to the present claims. Accordingly, the Examiner is respectfully requested to remove this reference as a ground for rejection under 35 U.S.C. § 103.

As noted above, Capon et al. does not anticipate nor render obvious the current claims because this reference teaches only the use of a saturating concentration of the inducer FKBP, which the Examiner has agreed would not be ineffective in inducing dimerization of the chimeric receptors. Thus, Capon alone is insufficient to render the claims obvious.

In view of the above, applicants have shown that the invention of claims 1-42, 59-66 and 70-76 are not obvious over the combination of Capon et al. and Blau et al. Accordingly, the Examiner is respectfully requested to remove this ground for the rejection of these claims.

Rejections over Capon et al. in view of Crabtree et al. and Blau et al.

Claims 44-53 and 55-58 have been rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,741,899 (Capon et al.) in view of U.S. Patent No. 5,994,313 (Crabtree et al.) and Blau et al. (1997). The claims rejected over this combination of references in essence pertain to genetically engineered primary cells containing a recombinant DNA that encodes a fusion protein having a signaling domain and a drug-binding domain, or to methods of treatment comprising the introduction of such genetically engineered cells. As explained above, Blau et al. is not prior art with respect to the present application. Therefore, the sufficiency of this rejection rests on whether the claims are obvious over the combination of Capon et al. and Crabtree et al. .

The Examiner details the basis for this rejection at pages 7-11 of the Office Action of 10/06/05. In that Office Action, the Examiner notes that Capon et al. differs from the instant

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

invention by teaching only a saturating concentration of inducer. The Examiner acknowledges that the applicants have shown that a saturating amount of inducer is ineffective in inducing dimerization of the chimeric receptors. In rejecting the claims over Capon, Blau et al. and Crabtree et al., the Examiner has relied on both Crabtree et al. and Blau et al. for teaching methods for varying and optimizing the concentration of FKBP12 (see Office Action of 10/6/05, at page 9). However, the Examiner relies solely on Blau et al. for actually demonstrating concentrations of FK1012 that are effective to induce the association of the chimeric protein on cells to induce cell proliferation (see page 10 of Office Action of 10/6/05). Furthermore, the Examiner relies solely on Blau et al. to substantiate a reasonable expectation of success because of the "successful demonstration in Blau et al. of the testing methods and the identification of actual concentrations of FK1012 which were effective in inducing cell proliferation in cells expressing the chimeric protein." No such demonstrations are provided by Crabtree et al. nor by Capon et al. As noted above, Blau et al. is not prior art to the present application. The combined teachings of Capon and Crabtree et al. taken alone do not support a reasonable expectation of success.

Without Blau et al., the combined teachings of Capon et al. and Crabtree et al. do not render obvious the invention described in Claims 44-53 and 55-58. As applicants have pointed out before, if one skilled in the art simply followed the teachings of Capon et al., they would find that the assays taught therein did not work. Confronted with this failure, the skilled artisan would not know why the assays failed. As applicants have noted before, there could be many reasons why the assay did not work, given that Capon et al. did not provide any examples other than prophetic examples to demonstrate the functionality of the described chimeric proteins. Since Blau et al. is not prior art, this reference cannot be relied upon to demonstrate the functionality of the chimeric proteins. Thus, one following the teachings of Capon et al. would

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

have to experiment with various parameters of the assay to discover for themselves why it did not work. For example, there could be a problem with the dimerizing agent itself. If the dimerizing drug does not bring the chimeric proteins sufficiently close to one another, or alternatively, brings them too close to one another, signal transduction would not occur. Additionally, fusing a signaling domain to a heterologous inducing domain might, upon dimerization, orient the signaling domain in a way that prevents it from assuming the conformation necessary to transmit a signal. Since Capon et al. did not demonstrate the actual functionality of any of the described constructs, it would be reasonable for one skilled in the art, faced with a failed assay, to question whether the constructs were capable of functioning at all. In view of these considerations, it is unreasonable to assume that one skilled in the art would know to solve the problem by addressing the concentration of inducing drug as taught by Crabtree et al.

The Examiner asserts that Crabtree et al. supplements Capon et al. by teaching chimeric proteins comprising an inducer-responsive clustering domain and a signaling domain wherein the inducer-responsive domain of FKBP12 contains specific amino acid changes as compared with the wild-type sequences. However, one skilled in the art would have no motivation to combine the teachings of Crabtree et al. with the teachings of Capon et al. Accordingly, the invention described herein is not obvious over Capon et al. taken in view of Crabtree et al..

In view of the above, it is believed that claims 44-53 and 55-58 are not obvious over the combination of Capon et al., Crabtree et al. and Blau et al. Accordingly, the Examiner is respectfully requested to withdraw the rejection of these claims over this group of references.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

CONCLUSION

In view of the foregoing remarks and amendments, Claims 1-42, 44-53, 55-66 and 70-76 are believed to be in condition for allowance. The Examiner therefore is respectfully requested to remove the remaining ground for rejection and to allow these claims. If any issues remain that can be expeditiously addressed in a telephone interview, the Examiner is urged to contact the undersigned at his direct dial number given below.

Respectfully submitted,

CHRISTENSEN O'CONNOR
JOHNSON KINDNESS[PLLC]

Verne A. Luckow, Ph.D.
Registration No. 45,950
Direct Dial No. 206.695.1645

I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a sealed envelope as first-class mail with postage thereon fully prepaid and addressed to Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the below date.

Date: November 6, 2006 Jeffrey Harbert

DXS:VAL:jh

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS[PLLC]
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100